

## **AMENDMENTS TO THE CLAIMS**

**1. (Original)**           A screening method for a compound, or a salt thereof, that promotes or inhibits the interaction between Rap1 and p30 and/or the binding of Rap1 with p30, which comprises:

(1) a process to allow

(a) a polypeptide selected from the group consisting of an active-form polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:2, an active-form polypeptide containing a point-mutated SEQ ID NO:2 amino acid sequence wherein the 12th glycine thereof is replaced with valine or an amino acid sequence essentially identical to said point-mutated amino acid sequence, a partial peptide thereof, and a salt thereof;

(b) a polypeptide selected from the group consisting of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4, a partial peptide thereof, and a salt thereof; and

(c) a test sample

to come in contact with one another; and

(2) a process to detect the interaction and/or binding between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

**2. (Original)**           The screening method according to claim 1, comprising:

(1) the process to allow a polypeptide selected from the group (a), a polypeptide selected from the group (b), and a test sample to come in contact with one another;

(2) the process to detect the occurrence of the interaction and/or binding between the polypeptide selected from the group (a) and the polypeptide selected from the group (b); and

(3) a process to select a compound that promotes and/or inhibits the interaction and/or binding between these polypeptides.

**3. (Currently amended)** The screening method according to claim 1 ~~or 2~~, wherein another peptide is fused to a polypeptide selected from the group (a) and/or a polypeptide selected from the group (b).

**4. (Currently amended)** The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide selected from the group (a) and/or the polypeptide selected from the group (b) is labeled and the label is detected or measured to detect the binding and/or interaction of the polypeptides.

**5. (Currently amended)** The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide of the group (b) bound to the polypeptide of the group (a) is assayed with a primary antibody against the polypeptide of the group (b) or a primary antibody against another peptide fused to the polypeptide of the group (b) to detect the binding and/or interaction between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

**6. (Currently amended)** The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide selected from the group (a) bound to the polypeptide selected from the group (b) is assayed with a primary antibody against the polypeptide of the group (a) or a primary antibody against another peptide fused to the polypeptide of the group (a) to detect the binding and/or interaction between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

**7. (Currently amended)** The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide selected from the group (b) bound to the polypeptide selected from the group (a) is assayed with a primary antibody against the polypeptide of the group (b) or a primary antibody against another peptide fused to the polypeptide of the group (b) and a secondary antibody against the primary antibody to detect the binding and/or interaction between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

**8. (Currently amended)** The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein

the polypeptide of the group (a) is an active-form fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:2 or an active fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having a point-mutated SEQ ID NO:2 amino acid sequence in which the 12th glycine thereof is replaced with valine; and

the polypeptide of the group (b) is a polypeptide, or a salt thereof, wherein an Myc epitope is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:4.

**9. (Original)** A screening kit for a compound, or a salt thereof, which promotes or inhibits the interaction and/or binding between Rap1 and p30 which comprises an effective amount of

(a) a polypeptide selected from the group consisting of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:2, and a polypeptide containing a point-mutated SEQ ID NO:2 amino acid sequence in which the 12th glycine thereof is replaced with valine, or an amino acid sequence essentially identical to said point-mutated amino acid sequence, a partial peptide thereof and a salt thereof; and

(b) a polypeptide selected from the group consisting of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4, a partial peptide thereof, and a salt thereof.

**10. (Original)** The screening kit according to claim 9, wherein another peptide is fused to the polypeptide selected from the group (a) and/or the polypeptide selected from the group (b).

**11. (Original)** The screening kit according to claim 9, wherein the polypeptide selected from the group (a) and/or the polypeptide selected from the group (b) is labeled.

**12. (Original)** The screening kit according to claim 9, wherein  
the polypeptide of the group (a) is a fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:2 or a fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having a point-mutated SEQ ID NO:2 amino acid sequence in which the 12th glycine thereof is replaced with valine; and

the polypeptide of the group (b) is a fusion polypeptide, or a salt thereof, wherein an Myc epitope is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:4.

**13. (Currently amended)** A compound, or a salt thereof, ~~with~~ which promotes or inhibits the interaction and/or binding between Rap1 and p30 and is obtained using the screening method according to claim 1 ~~or the screening kit according to claim 9.~~

**14. (Original)** The compound, or a salt thereof, according to claim 13 which inhibits the interaction and/or binding between Rap1 and p30.

**15. (Original)** A pharmaceutical composition containing the compound or the salt thereof according to claim 13.

**16. (Original)** A pharmaceutical composition comprising an effective amount of the compound, or a salt thereof, according to claim 14.

**17. (Currently amended)** The pharmaceutical composition according to claim 15 ~~or 16~~, wherein a target to be treated or prevented is selected from the group consisting of:

(a) inflammatory diseases;

(b) immune diseases;

- (c) graft versus host reaction upon organ transplantation; and
- (d) cancers.

**18. (Original)** A monoclonal antibody that recognizes a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4.

**19. (Original)** A diagnostic method which comprises using the monoclonal antibody according to claim 18.

**20. (Original)** A diagnostic kit which comprises an effective amount of the monoclonal antibody according to claim 18.

**21. (Original)** A polypeptide, or a salt thereof, that functions intracellularly against a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4 in a dominantly negative fashion.

**22. (Original)** A composition comprising an effective amount of the polypeptide, or a salt thereof, according to claim 21 for treatment or prevention of a disease selected from the group consisting of:

- (a) inflammatory diseases;
- (b) immune diseases;
- (c) graft versus host reaction on organ transplantation; and
- (d) cancers.

**23. (Original)** A polynucleotide encoding the polypeptide according to claim 21.

**24. (Original)** A composition comprising an effective amount of the polynucleotide according to claim 23 for treatment or prevention of a disease selected from the group consisting of:

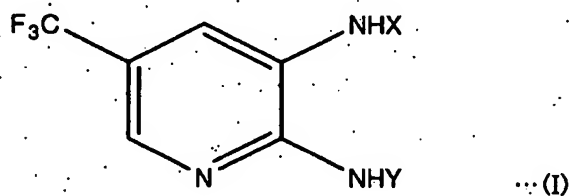
- (a) inflammatory diseases;
- (b) immune diseases;
- (c) graft versus host reaction upon organ transplantation; and
- (d) cancers.

**25. (Original)** A transgenic animal having a regulated expression of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:10.

**26. (Original)** The transgenic animal according to claim 25, wherein a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:10 is overexpressed.

**27. (Currently amended)** The transgenic animal according to claim 25 or 26, which is a mouse.

**28. (Original)** A Rap1-p30 binding inhibitor which comprises an effective amount of a compound, or a salt thereof, of the formula (I):



wherein X is a group:  $-CW^1R^1$  or  $-C(=W^1)W^2R^2$

in which

$R^1$  is alkyl, haloalkyl, alkoxycarbonylalkyl, alkenyl, haloalkenyl, alkenyl

substituted with thienyl, cycloalkyl, cycloalkyl substituted with a halogen atom, phenyl, phenyl substituted with a halogen atom, phenyl substituted with alkyl or haloalkyl, phenyl substituted with alkoxy or haloalkoxy, tetrahydronaphthyl, indanyl, furanyl, or thienyl,

$R^2$  is alkyl or haloalkyl, and

$W^1$  and  $W^2$  each independently represents an oxygen or sulfur atom, and

$Y$  is  $-SO_2R^9$

in which

$R^9$  is alkyl, haloalkyl, phenyl, phenyl substituted with a halogen atom, phenyl substituted with alkyl or haloalkyl, or phenyl substituted with alkoxy or haloalkoxy].

**29. (Original)** The Rap1-p30 binding inhibitor according to claim 28, wherein X is alkoxycarbonylalkylcarbonyl, alkenylcarbonyl, alkenylcarbonyl substituted with thienyl, cycloalkylcarbonyl, indanylcarbonyl, furancarbonyl, thiophenecarbonyl, tetrahydronaphthylcarbonyl, or benzoyl unsubstituted or optionally substituted with a halogen atom or haloalkyl, and Y is alkylsulfonyl.

**30. (Original)** The Rap1 and p30 binding inhibitor according to claim 28, wherein X is cycloalkylcarbonyl, furancarbonyl or benzoyl unsubstituted or optionally substituted with halogen, and Y is alkylsulfonyl.

**31. (Original)** The Rap1-p30 binding inhibitor according to claim 28, wherein the compound is selected from the group consisting of

N-(2-ethylsulfonylamino-5-trifluoromethyl-3-pyridyl)cyclohexanecarboxamide,  
N-(2-methylsulfonylamino-5-trifluoromethyl-3-pyridyl)-4-fluorobenzamide,  
N-(2-isopropylsulfonylamino-5-trifluoromethyl-3-pyridyl)-3-fluorobenzamide,  
N-(2-methylsulfonylamino-5-trifluoromethyl-3-pyridyl)-2-furancarboxamide, and  
N-(2-isopropylsulfonylamino-5-trifluoromethyl-3-pyridyl)cyclopentanecarboxamide.

**32. (Original)** A Rap1-p30 binding inhibitor comprising an effective amount of N-(2-ethylsulfonylamino-5-trifluoromethyl-3-pyridyl)cyclohexanecarboxamide or a salt thereof.

**33. (New)** A compound, or a salt thereof, ~~wieh~~ which promotes or inhibits the interaction and/or binding between Rap1 and p30 and is obtained using the screening kit according to claim 9.